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Case Report: Pulmonary Blastoma in Children—Response to Chemotherapy

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Pulmonary blastoma (PB) is a rare primary malignancy of the lung, with about 54 cases reported in children. The tumor consists of mesenchymal and epithelial components resembling the fetal lung. It has been treated primarily with surgery and the effect of combination chemotherapy has not been systematically investigated. A 15-year-old girl with PB with metastases to bone and regional lymph node, and high levels of alphafetoprotein, is reported. A preoperative combination chemotherapy consisting of cisplatinum, etoposide alternating with iphosphamide with mesna, vincristine and epirubicine resulted in an objective response that permitted subsequent safe surgical excision of the primary tumor. This intensive combination chemotherapy should be tested in the management of advanced PB in children, as initial therapy as well as an adjuvant to surgery.

Key words: pulmonary blastoma, children, chemotherapy, surgery, alphafetoprotein

INTRODUCTION

Pulmonary blastoma (PB) is a rare malignant tumor of the lung that consists of both primitive mesenchymal tissue and disordered epithelial tubules resembling fetal lung tissue [1,2]. Some authors [3,4] reported that PB in children before the age of 15 years is a different lesion from adult type PB and they call the childhood form pleuropulmonary blastoma. More than 150 cases have been reported in the literature, 54 occurring in children [2–11].

This tumor has been treated primarily with surgery alone with poor results. The role of radiation therapy has not been established and the effect of combined chemotherapy has not been systematically investigated. In this report, a girl with PB and bone and lymph node regional metastases and high levels of alphafetoprotein, was initially treated with combination chemotherapy that resulted in an objective response that permitted a safe and complete surgical excision of the primary tumor.

CASE REPORT

A 15-year-old female presented in November 1990 with a febrile illness associated with cough and right-sided chest pain that was treated as bronchitis. In April 1991 she was referred to the Oncology Department with the same symptoms. A visible and palpable hard tumor in the first right rib, clavicle, and sternal manubrium was found, with lymph nodes in the right supraclavicular region. A chest radiograph showed a large space-occupying solid mass in the right lower lobe of the lung of 9.6 cm and 9.3 cm of transverse and vertical diameter, respectively, another mass in the right side of the mediastinum and destruction of first right rib, clavicle and sternum. Computed tomographic (CT) scanning of the thorax confirmed the presence of a right lung high-attenuation solid tissue with the same measurement (Fig. 1). A bone scan demonstrated increased radiotracer uptake in first right rib, sternum, and clavicle. An abdominal ultrasonography was normal. A full blood count, urinary cathecolamines, hepatic and renal function studies were normal. The lactic dehydrogenase (LDH) was 380 μ/L (normal 180 μ/L), alpha fetoprotein (AFP) 100 ng/ml and carcinoembryonic antigen was 3 ng/ml. A biopsy of the supraclavicular nodes was performed and the histology showed tumor with two components: tubules and fusocellular stroma. It was reported as "malignant tumor metastases of primary tumor from posterior mediastinum: biphasic extrarenal Wilm's tumor or triphasic malignant teratoma."

Because of the high risk of a primary surgery and the presence of metastases, the patient was treated with 6

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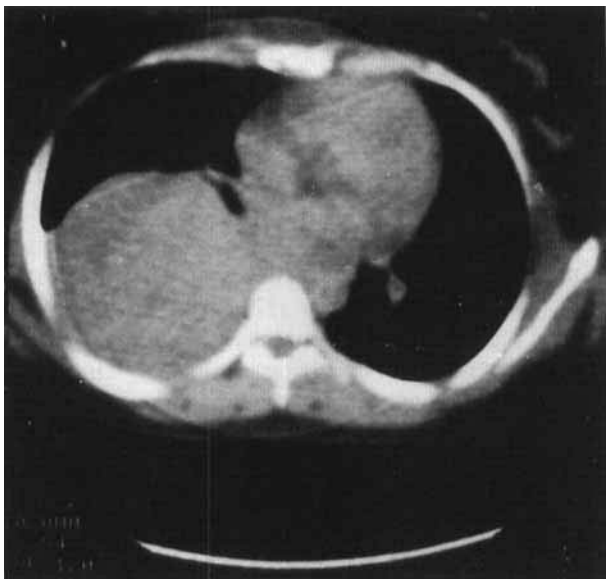

Fig. 1. CT scanning shows the tumor in the right hemithorax at the moment of diagnostic. Transverse diameter 9 cm.

monthly cycles of cisplatinum (CDDP) 100 mg/m^2/i.v. in five days, plus etoposide (VP16) 100 mg/m^2/i.v. alternating with iphosphamide (3 g/m^2/i.v. in three days with mesna), vincristine (VCR) 2 mg/m^2/i.v. and epirubicine (Epi) 50 mg/m^2/i.v. No serious toxic side effects were observed with chemotherapy. This resulted in complete pain relief and marked reduction in tenderness of rib, clavicle and sternum. A chest radiograph and CT scanning demonstrated that the bone lesions began to show sclerosis, and the pulmonary tumor measured half the original size (4.5 cm transverse diameter and 4 cm vertical diameter; Fig. 2). At the moment of the third cycle of chemotherapy the level of AFP was in 40 ng/ml, but increased in the following three months to 100 ng/ml (Fig. 3).

In October 1991, a thoracotomy was performed and a well-circumscribed tumor was demonstrated in the upper segment of right lower lobe. An uncomplicated lobectomy was performed. The inferior right lobe resected showed a tumor measuring 6 × 4.5 × 5 cm. The bronchus showed tumor in the lumen (Fig. 4). Histologically there were numerous glandular structures with pseudostratified to simple epithelium that sometimes formed morular structures (Figs. 5,6). These epithelial structures were separated by stroma composed of undifferentiated spindle cells (Fig. 7). The diagnosis was "pulmonary blastoma with mediastinal and supraclavicular lymph nodes and bone metastases."

Histologic material was sent for a second opinion to The Children's Memorial Hospital of Chicago where the Pathology Department confirmed the diagnosis of PB. Six more cycles of CDDP, VP16 alternating with Ifos, VCR and Epi at the same doses were administered. In March 1992, the patient presented with pain in right shoulder, and tender lymphadenopathy in the right supraclavicular region. Chest radiography showed a right pleural effusion. She was treated with palliative Co60 radiotherapy (30 Gy midplane/incident doses, respectively) and palliative chemotherapy with cyclophosphamide, Epi, actinomycin and VCR every three weeks for 5

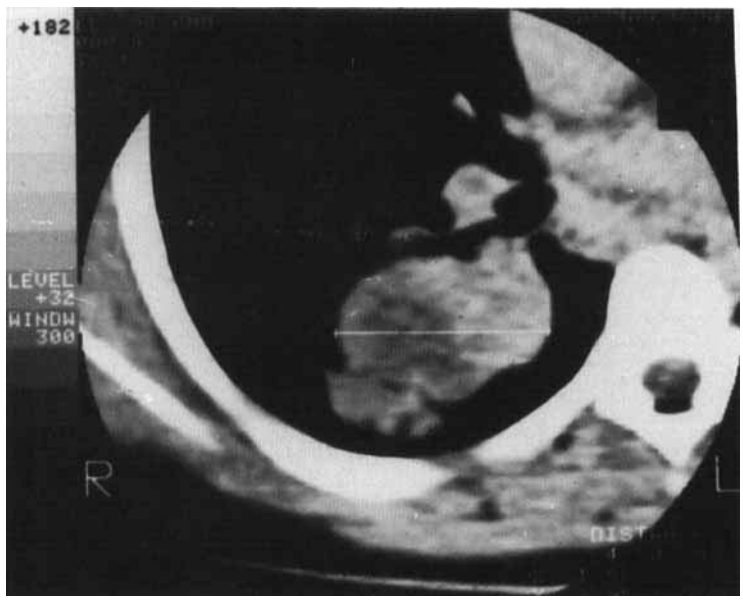

Fig. 2. Follow-up CT examination 6 months after chemotherapy shows marked reduction of the size of the tumor. Transverse diameter 4.5 cm.

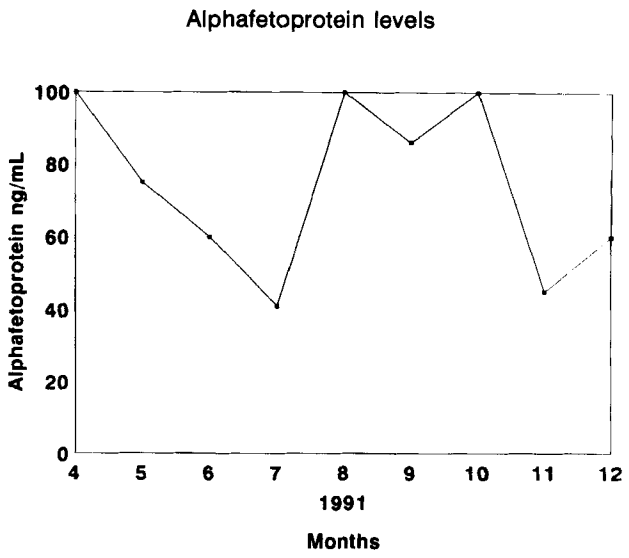

Fig. 3. Chart showing the levels of alphafetoprotein from diagnosis to clinical recurrence. The lower levels were in relation with the primary chemotherapy and tumor resection.

months, which resulted in marked clinical improvement. The mother then refused further active treatment and, two months later in October 1992, 18 months after the initial diagnosis, the patient died in her home from respiratory failure due to pleural effusion and clinical metastatic disease in mediastinum, cervical nodes, pleura, and bones. Consent for an autopsy was refused.

DISCUSSION

Pulmonary blastoma is a rare tumor of the lung in children with morphologic elements of immature blastema, stroma, and epithelium, all of neoplastic nature [1]. Approximately 54 cases are reported in the English literature in children younger than 16 years of age [2–11] with a slight male predilection. Although some patients have survived for a long time [8], prognosis is poor among those who have metastases or a primary tumor larger than 5 cm in diameter [12], like the present case. Manivel and Cohen [3,4] propose the existence of a intrathoracic neoplasm occurring exclusively in children under 15 years of age, that they named pleuropulmonary blastoma in which a malignant epithelial component is not present. In our case the tumor was present as an intraparenchymatous mass with the characteristic microscopic features including mesenchymal and epithelial components, which are morphologic elements of the adult-type PB. Of particular interest was the high levels of LDH and AFP maintained during evolution of the disease with decreased levels following initial chemotherapy and tumor resection, and the absence of malignant extraembryonic elements such as endodermal sinus tumor. Of all cases published as examples of pulmonary blastoma in children [2–14] there is not any report, to our knowledge, with high levels of AFP. Siegel et al. [15] describe two adult cases of PB having AFP production and histologic areas of yolk sac tumor. Abnormal levels of LDH have been reported by Koss et al. [2] in three of seven cases.

Surgery has always been the treatment of choice for pulmonary blastoma but there are relatively few reports

Fig. 4. Resected right pulmonary lower lobe which shows in its upper portion a tan and greyish white tumor with granular surface and partial necrosis with cystic spaces. The tumor invades the bronchus near the hilar region. The bronchial resection border was free of tumor.

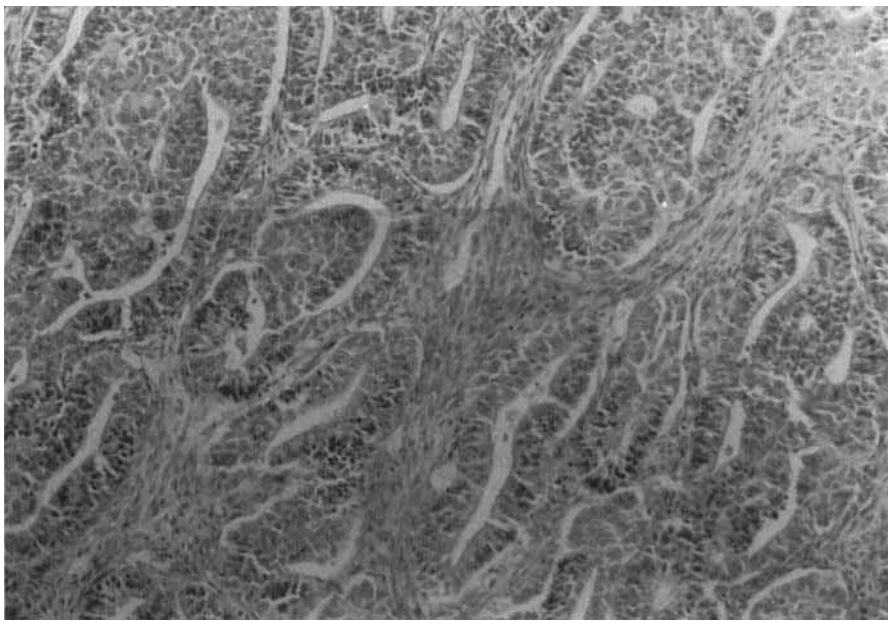

Fig. 5. Tubular structures separated by spindle-shaped stroma. H & E 100×.

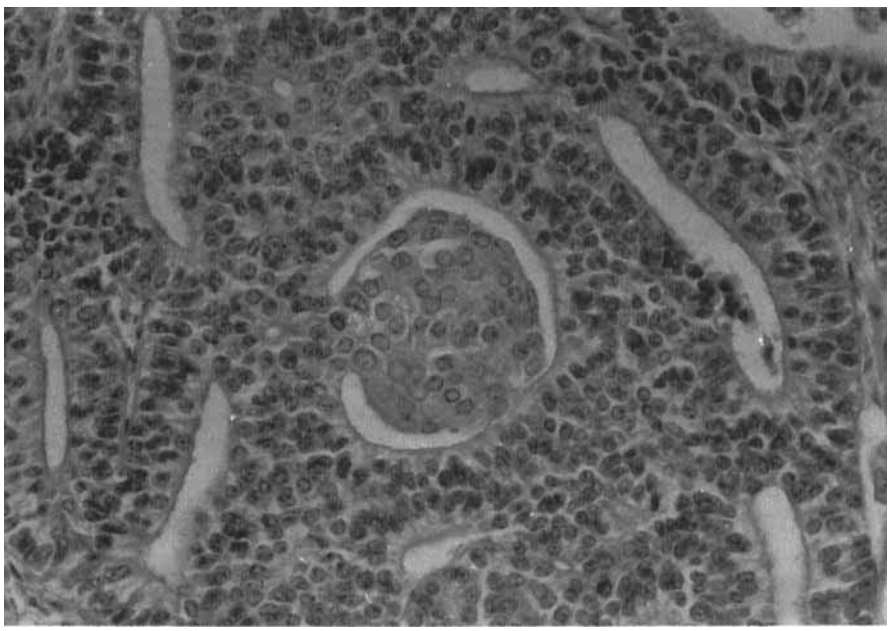

Fig. 6. Morular structures that could lead to erroneous diagnosis of metastases of extrarenal Wilm's tumor. H & E 200×.

in the literature about the value of chemotherapy [11,13]. Vincristine, dactinomycin, doxorubicin, and CFM were the most common frontline drugs with objective response in a few cases [6]. Ozkaynak et al. [11] reported two pediatric cases in whom combination chemotherapy consisting of VCR, actinomycin (ACTINO), cyclophosphamide (CFM), VP16, CDDP, and adriamycin (ADRIA) had successful results. One of these patients was initially treated and subsequently underwent surgical excision. In our patient, the size of the primary tumor greater than 5 cm and the metastases in bone and regional lymph nodes were signs of poor prognosis [12]. We consider the bone lesions of the clavicle and first rib to be metastatic because the primary tumor was in the lower lobe of the lung; there was no direct contact between this one and the superior chest wall and there was no pleural effusion at diagnosis. The use of CDDP, VP16, Ifos, Epi and VCR, as initial treatment, resulted in an objective response that

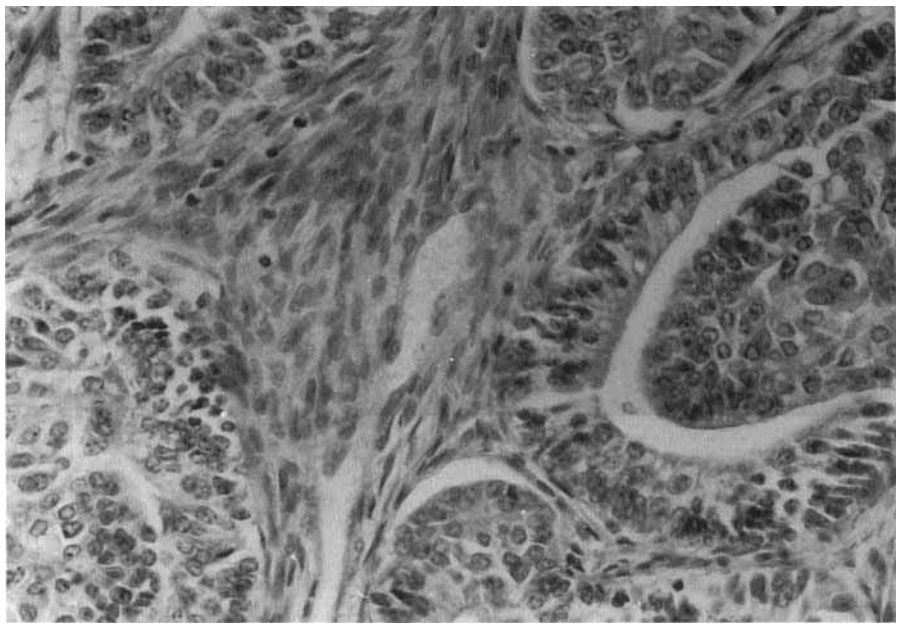

Fig. 7. Spindle-shaped cells of embryonic appearance form the tumoral stroma. H & E 200×.

permitted safe surgical excision of the primary tumor. The effectiveness of radiotherapy has not been established [14]. In the present case, good palliation of bone pain was rapidly achieved in the relapse phase with a dose of 30 Gy. Manivel et al. [3] reported two patients with pleuropulmonary blastoma treated with VCR, ACTINO, CFM, and radiotherapy who have a disease-free survival of 9 and 12 years, and two others with 14 and 32 months of survival.

We consider that, in patients with bulky tumors, multichemotherapy as initial therapy could diminish the risk of surgical complications and permit a complete surgical excision of the primary tumor in some cases. The use of adjuvant postsurgical multichemotherapy for control of the primary tumor and against probable distant metastases will be necessary to prolong the survival of these patients. More experience will be developed to determine a more effective therapy for children with this rare pathology.

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